DOCKET NO.: ISIS-4797 PATENT

Current Listing of Claims

1. (Currently Amended) A bi-phasic or multiphasic formulation comprising an aptamer, ribozyme, peptide nucleic acid, or antisense oligonucleotide or bioequivalent thereof having one or more phosphorothioate linkages, and a water-soluble anti-oxidant capable of inhibiting desulfurization of said oligonucleotide.

- 2. (Currently Amended) The formulation of claim 1, wherein said oligonucleotide or bioequivalent thereof comprises one or more base modifications.
- 3. (Currently Amended) The formulation of claim 1 wherein said oligonucleotide or bioequivalent thereof comprises one or more modified internucleoside linkages in addition to said one or more phosphorothioate linkages.
- 4. (Currently Amended) The formulation of claim 1, wherein said oligonucleotide or bioequivalent thereof comprises one or more sugar modifications.
- 5. (Original) The formulation of claim 4, wherein said sugar modification is a 2'-methoxyethoxy modification.
- 6. (Previously Presented) The formulation of claim 1, wherein said antioxidant is cysteine, glutathione, α -lipoic acid, a 2-mercapto-5-benzimidazole salt or a 2-mercaptoethanesulfonic acid salt.
- 7. (Currently Amended) The formulation of claim 1, wherein said oligonucleotide is a ribozyme, an aptamer or an antisense oligonucleotide.

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8. (Currently Amended) A method of preventing desulfurization of an aptamer, ribozyme, peptide nucleic acid, or antisense oligonucleotide or bioequivalent thereof comprising combining an the oligonucleotide having one or more phosphorothioate linkages with a water-soluble antioxidant in a bi-phasic or multi-phasic formulation.

- 9. (Currently Amended) The method of claim 8, wherein said oligonucleotide or bioequivalent thereof comprises one or more base modifications.
- 10. (Currently Amended) The method of claim 8, wherein said oligonucleotide or bioequivalent thereof comprises one or more modified internucleoside linkages in addition to said one or more phosphorothioate linkages.
- 11. (Currently Amended) The method of claim 8, wherein said oligonucleotide or bioequivalent thereof comprises one or more sugar modifications.
- 12. (Original) The method of claim 11, wherein said sugar modification is a 2'-methoxyethoxy.
- 13. (Previously Presented) The method of claim 8, wherein said antioxidant is cysteine, glutathione, α -lipoic acid, a 2-mercapto-5-benzimidazole salt or a 2-mercaptoethanesulfonic acid salt.
- 14. (Currently Amended) The method of claim 8, wherein said oligonucleotide is a ribozyme, <u>an</u> aptamer or <u>an</u> antisense oligonucleotide.